REMARKS

Claims 32-35 and 45-50 are listed as pending and rejected in the Summary of the January 7, 2009 Action.

Applicants request clarification of the status of claims 45-50. Page 2 of the Action states "It should be noted that the rejections have been somewhat modified to encompass all of the claims"; Applicants' October 24, 2008 Amendment listed claims 46-50 as not elected and thus withdrawn.

New claim 51 is claim 35, deleting cyclodextrin from the Markush group. No new matter is introduced.

CLAIM REJECTIONS UNDER 35 U.S.C. §112

Claims 32-35 and 45-50 are rejected under 35 U.S.C. §112 ¶1. The Examiner's position is that "...the specification, while being enabling for cyanine dyes, does not reasonably provide enablement for all photodiagnostic and phototherapeutic dyes..."

Claims 32-35 and 45 are rejected under 35 U.S.C. §112 ¶2 as indefinite. The Examiner states

> Specifically, review of the specification discloses that Applicant recognized a problem with cyanine dyes and proposes that the problem of aggregation/fluorescence be corrected by combining the dye with a biocompatible organic solvent at a concentration of 1-50% of solvent. However, the claims are not limited to cyanine dyes.

In response to both ¶¶ 1 and 2 rejections, Applicants have amended claim 32 to recite cyanine and indocyanine dyes.

The amendment introduces no new matter and is supported at least at p. 15 lines 17-21:

> The inventive bioconjugates of the present invention also exploit the symmetric nature of the cyanine and indocyanine dye structures by incorporating one to ten receptor-targeting groups in close proximity to each other, such that the receptor binding can be greatly enhanced due to a cooperative effect.

and p. 28 lines 18-20:

> The inventive compositions and methods represent an important approach to the synthesis and use of novel cyanine and indocyanine dyes with a variety of photophysical and chemical properties.

and formulas 1 and 3 disclosing cyanine dyes (defined in Hawley's Chemical Dictionary (attached) as

> Cyanine dye. One of a series of dyes consisting of two heterocyclic groups (usually quinoline nuclei) connected by a chain of conjugated double bonds containing an odd number of carbon atoms. Example: cyanine blue $C_2H_4NC_9H_6{:}CHC_9H_6NC_2H_2$. They include the isocyanines, merocyanines, cryptocyanines, and dicyanines. (Hawley's

Condensed Chemical Dictionary, 14th Ed., John Wiley & Sons, Inc. New York 2001))

and formulas 2 and 4 disclosing indocyanine dyes. Although the specification refers to formulas 2 and 4 as "cyanine" dyes (pp. 7, 11 respectively), a person of ordinary skill in the art appreciates that formulas 2 and 4 disclose indocyanine dyes, having two phenyl rings and being napthalene ($C_{10}H_8$) derivates.

Applicants thus assert the rejections under 35 U.S.C. §112 ¶¶1 and 2 are overcome and respectfully request their withdrawal.

CLAIM REJECTIONS UNDER 35 U.S.C. §103

Claims 32-35 are rejected under 35 U.S.C. §103(a) as obvious over Licha U.S. Patent No. 6,083,485.

The Examiner's modified rejection encompasses claims 32-35 over Licha, stating "Thus it would be obvious to a skilled artisan in the art to combine a cyanine dye with cyclodextrin ...".

Cyclodextrin is recited in only in dependent claim 35. Thus, Applicants respectfully request clarification whether the rejection applies to claims 32-35, or only claim 35.

Applicants respectfully disagree that "it would be obvious to a skilled artisan in the art to combine a cyanine dye with cyclodextrin and administer the compound to a subject because Licha et al disclose that cyclodextrin may be added to the dye."

As the Examiner states,

> The compounds of Licha et al are water soluble, tolerable, and stable in vitro and in vivo (column 8, lines 31-37). The dye mixture may be administered by intravenous injection and they [*sic*] irradiated with light (column 8, lines 42-49). In addition, Licha et al disclose that for cyanine dyes, increased solubility in water and the presences [*sic*] of hydrophilic groups suppress the formation of aggregates and micelles (column 13, lines 15-22).

Licha teaches adding cyclodextrin "for improving stability and solubility".

Based on Licha, a person of ordinary skill in the art would have no motivation to add cyclodextrin, because Licha teaches that the dyes should already be ones that are "well soluble in water" ("...dyes suitable for diagnostic purposes should be well soluble in water ...." (col. 3 lines 36-41), hence there would be no need to improve solubility.

Nonetheless, solely to expedite prosecution, Applicants have added claim 51 to delete cyclodextrin from the Markush group. Thus, claim 51 is not obvious over Licha.

Applicants respectfully assert for at least the above reasons, the rejection is overcome and requests its withdrawal.

CONCLUSION

Applicants believe the application is in complete condition for allowance. No fees are believed due but, if deemed necessary, the Office is authorized to charge them to Deposit Account No. 20-0809.

Respectfully submitted,

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Hawley's

Condensed Chemical Dictionary

Fourteenth Edition

Revised by

Richard J. Lewis, Sr.

JOHN WILEY & SONS, INC.

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converts the protein structure into a firm and durable product as a result of complexing reactions. See tanning. (3) Tobacco: Exposure for 3–5 days to temperatures from 37 to 65C to reduce moisture content, convert starches to reducing sugars, and discharge the chlorophyll, followed by aging from 1 to 5 years to remove odors and improve smoking quality.
(4) Cheese: Aging for 9–12 months at 4.5–10C to develop sharp flavor; the process is also called ripening.
(5) Rubber: Addition of sulfur and accelerator, followed by exposure to heat, which effects cross-linking. This converts the material from a thermoplastic to a thermosetting product. High-energy radiation can also be used. See vulcanization.

curium. Cm. Synthetic radioactive element of atomic number 96, aw 244, valences 3, 4. Isotopes available: 244 and 242 (gram quantities).
Properties: Silvery-white metal. D 13.5, mp 1340C. Chemically reactive. More electropositive than aluminum. An α emitter. Biologically it is a bone-seeking element. Forms compounds such as CmO_2, Cm_2O_3, CmF_3, CmF_4, $Cm(OH)_3$, $CmCl_3$, $CmBr_3$, $CmI_3 \bullet Cm_2(C_2O_4)_3$.
Use: Thermoelectric power generation for instrument operation in remote locations on earth or in space vehicles.
See actinide series.

Curl, Robert F., Jr. (1933–). An American who won the Nobel prize for chemistry along with Sir Harold W. Kroto and Richard E. Smalley in 1996, the 100th anniversary of Alfred Nobel's death. The trio won for the discovery of the C_{60} compound called buckminsterfullerene. He graduated from Rice University and received a Ph.D. from the University of California, Berkeley in 1957.
See buckminsterfullerene; Kroto, Sir Harold W.; Smalley, Richard E.

current density. In an electroplating bath or solution, the electric current per unit area of the object or surface being plated. Expressed in amperes per square centimeter or, more usually, amperes per square decimeter.

Curtius rearrangement. Formation of isocyanates by thermal decomposition of acyl azides.

cutback. A coating substance or varnish that has been diluted or thinned.

cutting fluid. A liquid applied to a cutting tool to assist in the machining operation by washing away the chips or serving as a lubricant or coolant. Commonly used cutting fluids are water, water solutions or emulsions of detergents and oils, mineral oils, fatty oils, chlorinated mineral oils, sulfurized mineral oils, and mixtures of the foregoing oils. Transparent grades are available.

"Cyana" *[Cytec].* TM used in connection with the textile finishes obtained by applying "Aerotex" resins and similar products.

"Cyanamer" *[Cytec].* TM for water-soluble polymers.
Use: Antiscalants, antiprecipitants, viscosity modifiers, corrosion inhibitors, and dispersants in a wide range of water treatment applications.

cyanamide. (1) (cyanogenamide; carbodiimide).
CAS: 420-04-2. HN:C:NH or $N:CNH_2$.
Properties: Deliquescent crystals. Mp 43C, d 1.08. Very soluble in water, alcohol, ether, phenols, ketones.
Hazard: Strong irritant to skin and mucous membranes; avoid inhalation or ingestion. TLV: 2 mg/m³.
(2) See calcium cyanamide.

cyanamide process. See nitrogen fixation; ammonia, anhydrous.

cyanic acid. See isocyanic acid.

cyanide pulp. The mixture obtained by grinding crude gold and silver ore and dissolving the precious metal content in sodium cyanide solution.

cyanine dye. One of a series of dyes consisting of two heterocyclic groups (usually quinoline nuclei) connected by a chain of conjugated double bonds containing an odd number of carbon atoms. Example: cyanine blue $C_2H_5NC_9H_6{:}CHC_9H_6NC_2H_5$. They include the isocyanines, merocyanines, cryptocyanines, and dicyanines.
Use: Sensitizers for photographic emulsions.

cyanoacetamide. (malonamide nitrile; propionamide nitrile). $CNCH_2CONH_2$.
Properties: White crystals. Mp 119C, bp (decomposes). Soluble in water and alcohol. Combustible.
Derivation: Ammonolysis of cyanoacetic ester or dehydration of ammonium cyanoacetate.
Hazard: Toxic by ingestion.
Use: Organic pharmaceutical synthesis, plastics.

cyanoacetic acid. (malonic nitrile). $CNCH_2COOH$.
Properties: White crystals, hygroscopic. Mp 66.1–66.4C; decomposes at 160C. Soluble in water, alcohol, and ether.
Derivation: Interaction of sodium chloroacetate and potassium cyanide solution.
Hazard: Toxic by ingestion.
Use: Organic synthesis.

cyanoacrylate adhesive. An adhesive based on the alkyl 2-cyanoacrylates (see for example methyl 2-cyanoacrylate). The latter are prepared by pyrolyzing the poly(alkyl)-2-cyanoacrylates pro-